PATENT COOPERATION TREA[illegible]

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
MARK FARBER
ALEXION PHARMACEUTICALS, INC.
352 KNOTTER DRIVE
CHESHIRE, CT 06410

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing (*day/month/year*) 19 OCT 2004
Applicant's or agent's file reference 106PCT	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/17219	28 May 2004 (28.05.2004)	02 June 2003 (02.06.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 39/395; CO7K 16/00; C12N 15/13 and US Cl.: 530/387.3; 424/133.1; 536/23.53; 435/69.6

Applicant

1. This opinion contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Ron Schwadron, Ph.D. J. Roberts for Telephone No. 571-272-1600

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/17219

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/17219

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. Claims 2,3,,8,9,14,15,18-20 were not examined because no CRF has been submitted

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☒ the claims, or said claims Nos. 2,3,8,9,14,15,18-20 are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/17219

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	5,16	YES
	Claims	1,4,6,7,10-13,17	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1,4-6,7,10-13,16,17	NO
Industrial applicability (IA)	Claims	1,4-7,10-13,16,17	YES
	Claims	NONE	NO

2. Citations and explanations:

Please See Continuation Sheet

International application No.
PCT/US04/17219

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:
Claims 1,4,6,7,10-13,17 lack novelty under PCT Article 33(2) as being anticipated by US Patent 6,491,916.

US Patent 6,491,916 discloses a "de-immunized" antiCD3 antibody where said antibody is de-immunized as per the definition of said term on page 5, first complete paragraph of the description (see abstract and column 15, last paragraph, and column 16, first paragraph). US Patent 6,491,916 discloses a nucleic acid encoding said antibody (see Example 3). Said antibody has deimmunized heavy and light chains (see column 16, first paragraph). US Patent 6,491,916 teaches expression vectors containing the aformentioned nucleic acids and use of said vectors to recombinantly produce said antibody (see Examples 4 and 5). US Patent 6,491,916 discloses pharmaceutical compositions containing said antibody (see column 18). US Patent 6,491,916 teaches administering said antibody (see column 18) and that said antibody can have a portion of a human IgG2 and portion of an IgG4 antibody (see column 16, last paragraph and column 17).

Claims 1,4-6,7,10-13,16,17 an inventive step under PCT Article 33(3) as being obvious over US Patent 6,491,916 in view of US Patent Application Publication 2003/0100741.

US Patent 6,491,916 discloses a "de-immunized" antiCD3 antibody where said antibody is de-immunized as per the definition of said term on page 5, first complete paragraph of the description (see abstract and column 15, last paragraph, and column 16, first paragraph). US Patent 6,491,916 discloses a nucleic acid encoding said antibody (see Example 3). Said antibody has deimmunized heavy and light chains (see column 16, first paragraph). US Patent 6,491,916 teaches expression vectors containing the aformentioned nucleic acids and use of said vectors to recombinantly produce said antibody (see Examples 4 and 5). US Patent 6,491,916 discloses pharmaceutical compositions containing said antibody (see column 18). US Patent 6,491,916 teaches administering said antibody (see column 18) and that said antibody can have a portion of a human IgG2 and portion of an IgG4 antibody (see column 16, last paragraph and column 17). While US Patent 6,491,916 does not specifically recite the method of claim 5,16, US Patent Application Publication 2003/0100741 discloses that de-immunized antibody can be made by removing or altering murine antigenic residues. Thus, any residual immune response to the antibody of 6,491,916 could be completely removed by deimmunizing said antibody wherein "antigenic residues" would encompass residues recognized by T cells.

Claims 1, 4-7, 10-13, and 16-17 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry. laims 1,4,6,7,10-13,17 lack novelty under PCT Article 33(2) as being anticipated by US Patent 6,491,916.

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